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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,245	07/26/2005	Neil Russell Foster	HILLS1130	8721

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EXAMINER	
THEODORE, MACIALI P	

ART UNIT	PAPER NUMBER
1791	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,245	FOSTER ET AL.	
	Examiner	Art Unit	
	Magali P. Théodore	1791	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12-14,16-18,20-24,26-33 and 38-41* is/are pending in the application.

4a) Of the above claim(s) *20-24,26-33 and 38-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,12-14 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed April 8, 2009 was received.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

The drawings were received on April 8, 2009. These drawings are acceptable.

Claim Rejections - 35 USC § 103

Claims 1, 3-6, 8-12 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerč et al. (International Journal of Pharmaceutics, 182 (1999), pp 33-39) henceforth **Kerč** in view of Kropf et al. (US 6,316,030 B1), henceforth **Kropf,** Jung et al. (Journal of Supercritical Fluids 20 (2001) 179-219), henceforth **Jung**, and Weidner et al. (US 6,056,791), henceforth **Weidner**.

Regarding **claim 1**, Kerč discloses a method of working with fenofibrate (page 34 left, last paragraph, line 3). Kerč teaches providing a pressure chamber (autoclave, figure 1 at A) with an inlet and an outlet. Kerč teaches applying a liquefied gas (supercritical carbon dioxide, title) to a mixture of fenofibrate and a carrier (page 35 right, section 2.2 top) and heating the mixture close to but lower than the drug's atmospheric melting point (page 35 right, section 2.2 bottom) until the mixture is melted (page 35 right, section 2.2 line 2). Kerč teaches equilibrating the substance and the liquefied gas to form a homogeneous solution (page 35 left lines 2-3). Then the mixture

is sent to a vessel of lower pressure (expansion chamber, figure 1 at C) where particles form.

Kerč does not positively state that the fenofibrate is solid before it meets the liquefied gas or that the liquefied gas melts the fenofibrate. However, Kropf teaches making particles by applying a liquefied gas (carbon dioxide, page 3 lines 16-19) to a solid substance ("melted by the introduction of gas," page 3 line 17) and then taking the solution to an environment of reduced pressure ("expansion through a nozzle") to form particles of the substance (page 3 lines 23-24). The melting point of the substance is depressed in the presence of the supercritical gas (page 3 lines 20). The step explicitly taught by Kropf is an effective alternative to melting the drug before introducing the liquefied gas. Therefore it would have been obvious to one of ordinary skill in the art to use the liquefied gas to melt solid fenofibrate in the method taught by Kerč, either by combining Kropf's teaching with the steps in Kerč's as they are explicitly disclosed or by substituting Kropf's melting step for a pre-melting step.

Kerč does not teach that the pressure chamber's outlet is above its inlet. However, Jung teaches mixing compressed carbon dioxide with an active substance a pressure chamber whose outlet is above its inlet (precipitator, page 188 figure 2). Though Jung is practicing an anti-solvent process (page 187 middle heading), Jung's reasoning for introducing the compressed gas from the bottom of the vessel is applicable in PGSS: to achieve better mixing as the gas travels upward (page 188 first paragraph). Therefore it would have been obvious to one of ordinary skill in the art to

use place the outlet in Kerč's method above the inlet in order to provide for better mixing of the ingredients.

Kerč does not teach using a carrier fluid at the same pressure as the liquefied gas to pass the molten substance-gas solution out through the outlet. However, Weidner teaches contacting the solution with "fresh, preheated gas" to maintain the pressure that pushes the solution out from the pressure chamber (column 8 lines 18-21). Therefore, it would have been obvious to one of ordinary skill in the art to use a carrier fluid in the method taught by Kerč because Weidner teaches doing so in order to maintain the expelling pressure in the pressure chamber. *Alternatively*, it would have been obvious to one of ordinary skill in the art to combine the use of a carrier fluid with the steps taught by Kerč in order to achieve predictable results with a reasonable expectation of success.

Regarding **claim 3**, Kerč does not explicitly teach that the carrier is the same as the liquefied gas. However, Kerč presents the carrier as optional (page 34 section 2.2 line 3) and shows the liquefied gas acting as a carrier fluid by carrying the drug into the expansion chamber (figure 1). Therefore, it would have been obvious to one of ordinary skill in the art to use the same gas as the liquefied gas and the carrier fluid because Kerč discloses the liquefied gas acting as a carrier fluid.

Regarding **claims 4-5**, Kerč teaches allowing the substance and the liquefied gas to equilibrate for about two hours before spraying (page 35 left lines 2-3). Kerč does not specify equilibrating *before* adding the carrier. However, selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected

results and selection of any order of mixing ingredients is prima facie obvious (MPEP 2144.04 IIC). Therefore it would have been obvious to one of ordinary skill in the art to equilibrate the drug and the liquefied gas for two hours before introducing the carrier because Kerč teaches both those steps.

Regarding **claim 6**, fenofibrate is a pharmaceutical agent (a hypolipidemic, Abstract).

Regarding **claim 8**, Kerč teaches that the temperature is between 5 ºC and 150 ºC (70 ºC, page 38 left line 6).

Regarding **claim 9**, Kerč teaches that the pressure of the liquefied gas and the carrier fluid is between 5 bar and 200 bar (190 bar, page 38 left line 6).

Regarding **claim 10**, Kerč teaches that the liquefied gas is carbon dioxide (title).

Regarding **claims 12-13**, Kerč does not teach the particle sizes specified by the claims. However, Kerč teaches that particle size determines the drug's dissolution rate and bioavailability. Therefore it would have been obvious to one of ordinary skill in the art to optimize the particle sizes in order to control the drug's dissolution and absorption by the body. Optimizing a result-effective parameter known in the art does not impart patentable distinction to an invention. See MPEP 2144.05 [R-5] II, in re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Regarding **claim 39**, Kerč teaches that the substance is fenofibrate (page 34 left, last paragraph, line 3).

Claims 7, 14 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerč in view of Kropf as applied to claims 1 and 6 above, and further in view of Zhu et al. (US 2002/0110526 A1), henceforth **Zhu**.

Regarding **claim 7**, Kerč does not teach applying this method to cyclosporine. However, Zhu teaches using supercritical fluid technology ([0059] lines 10-12) to make slow-release coated particles of cyclosporine ([0020] second-to-last line). Therefore, it would have been obvious to one of ordinary skill in the art to substitute cyclosporine for the fenofibrate taught by Kerč because Zhu teaches that cyclosporine is a suitable material to micronize by treating it with a liquefied gas.

Regarding **claims 14** and **16-18**, Kerč does not address encapsulation. However, Zhu teaches using supercritical fluid technology ([0059] lines 10-12) to encapsulate drug particles with biodegradable, slow-release polymers like poly(d,l-lactide-co-glycolide) ([0005] line 3] and cellulose ([0040] penultimate line) in order to preserve the drug as it makes its way into the body ([0004]). Therefore it would have been obvious to one of ordinary skill in the art to incorporate encapsulation with biodegradable slow-release polymers into the supercritical fluid method taught by Kerč because Zhu teaches doing so to preserve the activity of the drug.

Response to Arguments

Applicant's arguments with respect to claim 1 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magali P. Théodore whose telephone number is (571) 270-3960. The examiner can normally be reached on Monday through Friday 9:00 a.m. to 6:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina A. Johnson can be reached on (571) 272-1176. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Magali P. Théodore/
Examiner, Art Unit 1791

/Christina Johnson/

Supervisory Patent Examiner, Art Unit 1791